AGGGAGAGTCTGCCCACAAGTTTTTGTATATTTTCTCACTGAGGCATCTATTCAGTTTGGGCAGCAGACA
CTGAGCAGAACGTAGCACGGCAATGCTTGGTAGCAATGCCTGTCCGGCCAGCACTCAGAAGACGGAGGCA
GGAGAATCATAGCTTCCAGTCAGCCTCTTCTACAATATAGTCAGTTGGAAGTCAGCCAGCTTAGACAACA
TGGAGAGCCTGTGCCGAAAGCCACTGGGTAAGCCCGAATCTCAGTAGCAGAGAGCTGCCCAGGGTGCGTA
CTGC:AAAAAAAAAACCTCAAACAACAGAAGTAGGGAGGTGTAAAATAAAGTGTAGGGGGGTGGAATTTA
AGCTGATGTGGACTTCCAAATAAAGTTACCTTTTAGATACCTATTTAAATCAATAGCATAGACCTGAAAC
TGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGGGGCCTCTGGCT
TTGAGAGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTTATAAATTCACCATGAGCTTTAAC
ATCTTCTTTGTCATTTCGCAGACTGAGCCATGGAGTCTTTCGATGCTGACACCAATTCAACTGACCTACA
CTCACGGCCTCTGTTTCAACCCCAAGACATTGCCTCCATGGTCATTCTTGGTCTCACTTGTCTATTGGGA
CTGCTAGGCAATGGGCTGGTGCTGTGGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGT
TCCTCCATCTCACCCTGGCCGATTTCCTCTGCTGCCTCTCCTTGCCCTTCTCCTTGGCTCACCTGATTCT
CCAAGGACACTGGCCCTATGGCTTGTTCCTGTGCAAACTTATCCCATCCATCATTATTCTCAACATGTTT
GCCAGTGTCTTCCTGCTTACTGCCATTAGCCTGGACCGATGTCTGATAGTACATAAGCCAATCTGGTGCC
AGAATCATCGAAACGTGAGAACCGCCTTCGCCATCTGTGGATGTGTCTGGGTGGTAGCCTTTGTGATGTG
TGTGCCCGTATTTGTATACCGTGATCTGTTCATTATGGACAATCGCAGTATATGTAGATATAATTTTGAT
TCCTCCAGGTCATATGATTATTGGGACTACGTGTACAAACTAAGTCTACCAGAAAGCAATTCTACTGATA
ACTCCACTGCTCAGCTAACTGGACATATGAATGACAGGTCAGCTCCTTCCTCTGTACAGGCAAGGGATTA
CTTTTGGACAGTTACCACTGCCCTCCAGTCACAGCCATTCCTAACATCTCCTGAAGACTCATTCTCTCTA
GATTCAGCAAACCAACAACCCCATTATGGTGGAAAGCCTCCTAATGTCCTCACAGCCGCCGTACCCAGCG
GGTTCCTGTTGAAGATCGTAAATCCAATACACTGAACGCTGACGCTTTTCTCTCTGCTCACACAGAACT
TTTCCCTACTGCTTCTAGTGGTCATTTATACCCCTATGATTTCCAGGGGGATTATGTTGACCAATTCACG
TATGACAATCATGTGCCGACACCGCTGATGGCAATAACCATCACAAGGCTGGTGGTGGGCTTCCTGGTGC
CGTTTTTCATCATGGTAATTTGTTACAGCCTCATCGTCTTCAGAATGCGAAAAACCAACTTCACCAAGTC
TCGGAACAAAACCTTTCGGGTGGCTGTGGCTGTGGTCACTGTCTTTTTTATCTGCTGGACTCCATACCAT
CTTGTCGGAGTCCTGCTATTGATTACTGATCCAGAAAGTTCCTTGGGGGAAGCTGTGATGTCCTGGGACC
ACATGTCCATTGCTTTAGCATCTGCCAATAGTTGCTTCAACCCTTTCCTGTATGCCCTCTTGGGGAAAGA
CTTTAGGAAGAAAGCAAGACAGTCTATAAAGGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCAC
TCTACCAACTGTACCCAAGACAAAGCCTCTTCAAAAAGAAACAATATGAGTACAGATGTGTGAAGATGTG
GCCCTGGGAACCTAAGCAGAGTTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTTAGACA
ATTTGGCGACTCTCAGAGAAAGGTCTCTTATTGACATCAGCATCATTTGAAAACATTAAAGATGCAAAT
TTCAAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGGCCCATGGGACCAGTGTTTTAACAGGCCTTC
TTGTTTCCATCAGTGTTAAGTTTTACCTCATTTGGCTTAGTCTATTCCCATCCCTGACTACACCATGTGC
AATGAATAACTTTTTCATCTGTTTTCAGTATTCTTTTTTTTTCCTTAGCATCATCTAAACTTCTAGTTTG
CATGGAAGGCTGCTCTTATTGTTCTGAATGGAAGATATTCATTTATTGTACAGTTTTGTGGTGGTGACAA
GTGATTTTTAAGTGGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTTGAGTTAGAGT
TTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATTCCAGTGTTCATGTGAGCA
AGTGAGCACAGATACACATAAACACTTTCCTACTCCTGGAGTGTTTTAGAAGTTGTAGCTTGGAGCTC
(SEQ ID NO:1)

MESFDADTNSTDLHSRPLFQPQDIASMVILGLTCLLGLLGNGLVLWVAGVKMKTTVNTVWFLHLT

LADFLCCLSLPFSLAHLILQGHWPYGLFLCKLIPSIIILNMFASVFLLTAISLDRCLIVHKPIWCQNHR

NVRTAFAICGCVWVVAFVMCVPVFVYRDLFIMDNRSICRYNFDSSRSYDYWDYVYKLSLPESNS

TDNSTAQLTGHMNDRSAPSSVQARDYFWTVTTALQSQPFLTSPEDSFSLDSANQQPHYGGKPP

NVLTAAVPSGFPVEDRKSNTLNADAFLSAHTELFPTASSGHLYPYDFQGDYVDQFTYDNHVPTP

LMAITITRLVVGFLVPFFIMVICYSLIVFRMRKTNFTKSRNKTFRVAVAVVTVFFICWTPYHLVGVLL

LITDPESSLGEAVMSWDHMSIALASANSCFNPFLYALLGKDFRKKARQSIKGILEAAFSEELTHST

NCTQDKASSKRNNMSTDV (SEQ ID NO:2)

FIG. 1

underlined = deleted in targeting construct

[ ] = sequence flanking Neo insert in targeting construct

AGGGAGAGTCTGCCCACAAGTTTTTGTATATTTTCTCACTGAGGCATCTATTCAGTTTGG
GCAGCAGACACTGAGCAGAACGTAGCACGGCAATGCTTGGTAGCAATGCCTGTCCGGCCA
GCACTCAGAAGACGGAGGCAGGAGAATCATAGCTTCCAGTCAGCCTCTTCTACAATATAG
TCAGTTGGAAGTCAGCCAGCTTAGACAACATGGAGAGCCTGT[GCCGAAAGCCACTGGGTA
AGCCCGAATCTCAGTAGCAGAGAGCTGCCCAGGGTGCGTACTGC:AAAAAAAAAACCTCA
AACAACAGAAGTAGGGAGGTGTAAAATAAAGTGTAGGGGGGTGGAATTTAAGCTGATGTG
GACTTCCAAATAAAGTTACCTTTTAGATACCTATTTAAATCAATAGCATAGACCTGAAAC
TGTCTATCAGAAAATGTGTCTATTCTGAGGAAGGAGTGCTAACGAGGTTCTGTGAGGGGG
GCCTCTGGCTTTGAGAGGGTGTACCATCACATAAGACTCCTAAAAGCACATACTTTTATA
AATTCACCATGAGCTTTAACATCTTCTTTGTCATTTCGCAGACTGAGCCATGGAGTCTTT
CGATGCTGACACCAATTCAACTGACCTACACTCACGGCCTCTGTTTCAACCCCAAGACAT
TG]CCTCCATGGTCATTCTTGGTCTCACTTGTCTATTGGGACTGCTAGGCAATGGGCTGGT
GCTGTGGGTAGCTGGCGTAAAGATGAAGACGACCGTGAACACAGTCTGGTTCCTCCATCT
CACCCTGGCCGATTTCCTCTGCTGCCTCTCCTTGCCCTTCTCCTTGGCTCACCTGATTCT
CCAAGGACACTGGCCCTAT[GGCTTGTTCCTGTGCAAACTTATCCCATCCATCATTATTCT
CAACATGTTTGCCAGTGTCTTCCTGCTTACTGCCATTAGCCTGGACCGATGTCTGATAGT
ACATAAGCCAATCTGGTGCCAGAATCATCGAAACGTGAGAACCGCCTTCGCCATCTGTGG
ATGTGTCTGGGTGGTAGCCTTTGTGATGTGTGTGCCCGTATTTGTATACCGTGATCTGTT
CATTATGGACAATCGCAGTATATGTAGATATAATTTTGATTCCTCCAGGTCATATGATTA
TTGGGACTACGTGT]ACAAACTAAGTCTACCAGAAAGCAATTCTACTGATAACTCCACTGC
TCAGCTAACTGGACATATGAATGACAGGTCAGCTCCTTCCTCTGTACAGGCAAGGGATTA
CTTTTGGACAGTTACCACTGCCCTCCAGTCACAGCCATTCCTAACATCTCCTGAAGACTC
ATTCTCTCTAGATTCAGCAAACCAACAACCCCATTATGGTGGAAAGCCTCCTAATGTCCT
CACAGCCGCCGTACCCAGCGGGTTTCCTGTTGAAGATCGTAAATCCAATACACTGAACGC
TGACGCTTTTCTCTCTGCTCACACAGAACTTTTCCCTACTGCTTCTAGTGGTCATTTATA
CCCCTATGATTTCCAGGGGGATTATGTTGACCAATTCACGTATGACAATCATGTGCCGAC
ACCGCTGATGGCAATAACCATCACAAGGCTGGTGGTGGGCTTCCTGGTGCCGTTTTTCAT
CATGGTAATTTGTTACAGCCTCATCGTCTTCAGAATGCGAAAAACCAACTTCACCAAGTC
TCGGAACAAAACCTTTCGGGTGGCTGTGTGGCTGTGGTCACTGTCTTTTTTATCTGCTGGAC
TCCATACCATCTTGTCGGAGTCCTGCTATTGATTACTGATCCAGAAAGTTCCTTGGGGGA
AGCTGTGATGTCCTGGGACCACATGTCCATTGCTTTAGCATCTGCCAATAGTTGCTTCAA
CCCTTTCCTGTATGCCCTCTTGGGGAAAGACTTTAGGAAGAAAGCAAGACAGTCTATAAA
GGGCATTCTGGAAGCAGCCTTCAGCGAAGAGCTCACGCACTCTACCAACTGTACCCAAGA
CAAAGCCTCTTCAAAAAGAAACAATATGAGTACAGATGTGTGAAGATGTGGCCCTGGGAA
CCTAAGCAGAGTTCTCAGGTGAACAGTGATGGATGACATGTGAGCAGGACACTTTAGACA
ATTTGGCGACTCTCAGAGAAAGGTCTCTTATTGACATCAGCATCATTTGAAAACATTAAA
GATGCAAAATTTCAAGCCCCATCCCAGATGTGTTGACTCAGAATCTCTGGCCCATGGGAC
CAGTGTTTTAACAGGCCTTCTTGTTTCCATCAGTGTTAAGTTTTACCTCATTTGGCTTAG
TCTATTCCCATCCCTGACTACACCATGTGCAATGAATAACTTTTTCATCTGTTTTCAGTA
TTCTTTTTTTTTCCTTAGCATCATCTAAACTTCTAGTTTGCATGGAAGGCTGCTCTTATT
GTTCTGAATGGAAGATATTCATTTATTGTACAGTTTTGTGGTGGTGACAAGTGATTTTTA
AGTGGGGAAAGAGACACAGTAAGAAAAGATCTATGAAAGCAGGGAGTGTTGAGTTAGAGT
TTGACAGAACACAGTGCCAAATGCCACCCACTAAAAGCAACCTGAGATAATTCCAGTGTT
CATGTGAGCAAGTGAGCACAGATACACATAAACACTTTCCTACTCCTGGAGTGTTTTAGA
AGTTGTAGCTTGGAGCTC

FIG. 2A

Gene Sequence Structure *

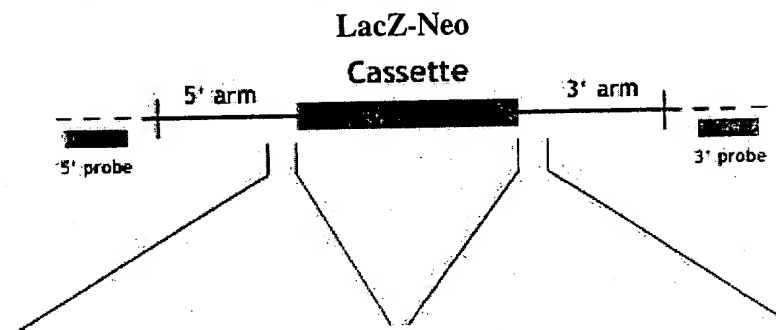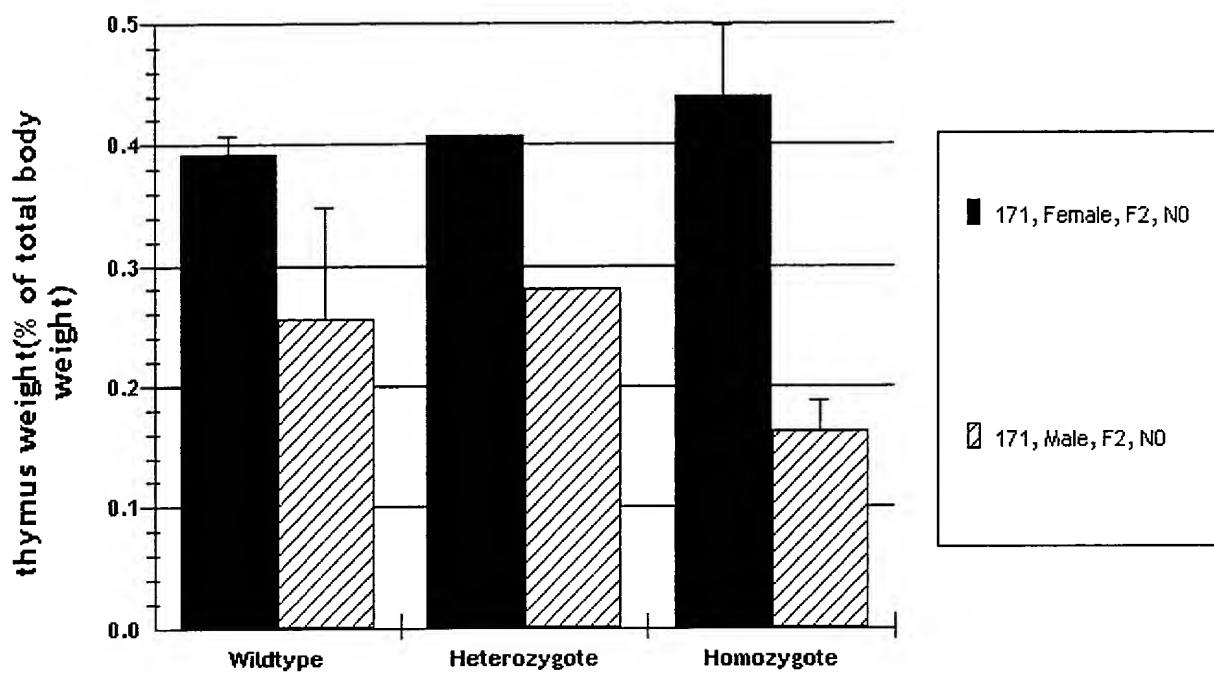663 bp   Sequence Deleted   859 bp

Size of full-length cDNA: 2658 bp

Targeting Vector* (genomic sequence)

Construct Number: 3036

LacZ-Neo Cassette

Arm Length:
5': 3.2 kb
3': 1.8 kb

————— Targeting Vector
- - - - - Endogenous Locus

Not drawn to scale

5' arm   Cassette   3' arm
5' probe   3' probe

5'>CGAGGTTCTGTGAGGGGGGCC
TCTGGCTTTGAGAGGGTGTACCAT
CACATAAGACTCCTAAAAGCACAT
ACTTTTATAAATTCACCATGAGCT
TTAACATCTTCTTTGTCATTTCGC
AGACTGAGCCATGGAGTCTTTCGA
TGCTGACACCAATTCAACTGACCT
ACACTCACGGCCTCTGTTTCAACC
CCAAGACATTG<3' (SEQ ID
NO:3)

5'>GGCTTGTTCCTGTGCAAACTT
ATCCCATCCATCATTATTCTCAAC
ATGTTTGCCAGTGTCTTCCTGCTT
ACTGCCATTAGCCTGGACCGATGT
CTGATAGTACATAAGCCAATCTGG
TGCCAGAATCATCGAAACGTGAGA
ACCGCCTTCGCCATCTGTGGATGT
GTCTGGGTGGTAGCCTTTGTGATG
TGTGTGCCCGT<3' (SEQ ID
NO:4)

FIG. 2B

necropsy - thymus weight/body weight

Legend:
- 171, Female, F2, N0
- 171, Male, F2, N0

Fig. 3